Section: General Medicine

Original Research Article

AUTONOMIC IMBALANCE IN CHRONIC KIDNEY DISEASE: A CROSS-SECTIONAL ANALYSIS OF HEART RATE VARIABILITY AND DISEASE PROGRESSION

Aedula Vibhav Prakash[1], Mohammed Akbar Ali[2], Taha Mahboob Ali Khalid[3]

[1]*Assistant professor, Department of General Medicine, Bhaskar Medical College, Telangana, India*
[2]*Associate professor, Department of General Medicine, Bhaskar Medical College, Telangana, India*
[3]*Associate Professor, Department of General Medicine, Bhaskar Medical College, Telangana, India*

Received *: 20/05/2025*
Received in revised form *: 07/07/2025*
Accepted *: 31/07/2025*

Corresponding Author:
Dr. Taha Mahboob Ali Khalid,
Associate professor, Department of General Medicine, Bhaskar Medical College, Telangana, India
Email: tahamak@gmail.com

DOI: 10.70034/ijmedph.2025.3.239

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (3); 1292-1296

ABSTRACT

Background: Chronic kidney disease (CKD) is a progressive condition associated with increased cardiovascular morbidity and mortality. Heart rate variability (HRV), a non-invasive marker of autonomic nervous system function, is often impaired in CKD patients, reflecting underlying autonomic dysfunction. Evaluating HRV in CKD patients may provide insight into their cardiovascular risk profile and guide early intervention.

Materials and Methods: This hospital-based cross-sectional study was conducted at the Department of General Medicine, Bhaskar Medical College and Bhaskar General Hospital, Telangana, India, from January 2024 to December 2024. A total of 120 participants were enrolled, including 90 CKD patients (stage 3–5) and 30 age- and sex-matched healthy controls. HRV was assessed using 5-minute resting ECG recordings, and time-domain and frequency-domain parameters were analyzed. Statistical analyses included unpaired t-tests, chi-square tests, and Pearson correlation with significance set at $p < 0.05$.

Results: CKD patients demonstrated significantly lower HRV across all indices: SDNN (23.6 ± 7.4 ms vs 41.2 ± 8.9 ms), RMSSD (18.2 ± 6.5 ms vs 34.6 ± 9.2 ms), LF (321.4 ± 108.2 ms² vs 548.6 ± 127.9 ms²), HF (212.7 ± 96.3 ms² vs 476.8 ± 132.5 ms²), and total power (654.2 ± 130.7 ms² vs 1021.4 ± 172.8 ms²), all $p < 0.001$. LF/HF ratio was elevated (2.61 ± 0.84 vs 1.21 ± 0.57, $p < 0.001$). HRV positively correlated with eGFR ($r = 0.58$ for SDNN, $p < 0.001$). Diabetic CKD patients had lower HRV than non-diabetics.

Conclusion: HRV is significantly reduced in CKD patients, especially those with comorbid diabetes, indicating a higher cardiovascular risk. HRV assessment can serve as a valuable, non-invasive screening tool for early identification of autonomic dysfunction in CKD patients.

Keywords: Chronic kidney disease, heart rate variability, cardiovascular risk, autonomic dysfunction, SDNN, LF/HF ratio.

INTRODUCTION

Chronic kidney disease (CKD) is a global health burden with rising prevalence, affecting approximately 10–15% of the adult population worldwide.[1] Characterized by progressive and irreversible loss of renal function, CKD is associated not only with renal complications but also with a substantially increased risk of cardiovascular morbidity and mortality.[2] Cardiovascular disease is the leading cause of death in patients with CKD, often occur prior to the need for renal replacement therapy.[3] This heightened risk is partly attributed to the autonomic nervous system (ANS) imbalance, which contributes to arrhythmias, sudden cardiac death, and left ventricular hypertrophy.[4]

Heart rate variability (HRV) is a non-invasive, quantitative marker used to evaluate the balance and modulation of the ANS by analyzing fluctuations in intervals between successive heartbeats (RR intervals).[5] Reduced HRV reflects sympathetic over-activity and parasympathetic withdrawal—an

autonomic state frequently observed in CKD patients.[6] Time-domain and frequency-domain indices derived from HRV analysis have been extensively used to stratify cardiovascular risk and autonomic dysfunction in various systemic conditions.[7] In the CKD population, HRV reduction is increasingly recognized as an early and independent predictor of cardiovascular events.[8]

Several pathophysiological mechanisms have been proposed for autonomic dysfunction in CKD, including chronic inflammation, oxidative stress, fluid overload, anemia, and endothelial dysfunction.[9] Additionally, comorbidities such as diabetes mellitus and hypertension, commonly seen in CKD patients, further aggravate autonomic imbalance.[10] Moreover, uremic toxins may have a direct neurotoxic effect on autonomic regulation, leading to diminished HRV even in early stages of renal impairment.[11]

Despite the established relevance of HRV as a predictor of adverse cardiovascular outcomes, its routine clinical use in nephrology remains limited. There is a need for more focused regional studies assessing HRV profiles in CKD patients to understand variations based on local demographics, comorbidities, and disease severity. Understanding HRV alterations in this high-risk group can help clinicians identify patients with subclinical cardiovascular dysfunction and initiate timely interventions to reduce complications.

The present study aims to evaluate HRV parameters in patients with moderate to severe CKD and compare them with healthy individuals. It also seeks to correlate HRV indices with disease severity and comorbid conditions, particularly diabetes and hypertension.

MATERIALS AND METHODS

Study Design and Setting: This was a hospital-based, observational, cross-sectional study conducted at the Department of General Medicine, Bhaskar Medical College and Bhaskar General Hospital, Telangana, India. The study was carried out over a 12-month period from January 2024 to December 2024.

Study Population: The study included a total of 120 participants, comprising 90 patients diagnosed with chronic kidney disease (CKD) stages 3 to 5 (non-dialysis) and 30 age- and sex-matched healthy controls. CKD diagnosis and staging were performed based on the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 guidelines, using estimated glomerular filtration rate (eGFR) calculated by the CKD-EPI equation.

Inclusion Criteria

- Age between 30 and 65 years
- CKD patients with eGFR <60 mL/min/1.73 m² for >3 months
- Written informed consent

Exclusion Criteria

- Current dialysis or history of renal transplantation
- Known ischemic heart disease or arrhythmias
- Patients on beta-blockers, antiarrhythmics, or antidepressants
- Acute infections, electrolyte imbalances, or thyroid dysfunction
- Uncontrolled diabetes (HbA1c > 9%) or uncontrolled hypertension

Data Collection and HRV Measurement: After obtaining informed written consent, demographic data (age, gender), clinical parameters (blood pressure, diabetes status, duration of CKD), and laboratory investigations (eGFR, hemoglobin, serum creatinine) were recorded.

HRV was assessed using a 5-minute resting ECG recording in the supine position, conducted in a quiet, temperature controlled room between 8:00 a.m. and 10:00 a.m. Participants were instructed to avoid caffeine, smoking, and strenuous activity for 12 hours prior to recording. Data acquisition and HRV analysis were conducted using standardized HRV software.

HRV Parameters Assessed

- Time-domain: SDNN (standard deviation of NN intervals), RMSSD (root mean square of successive RR differences)
- Frequency-domain: LF (low frequency), HF (high frequency), LF/HF ratio, Total Power

All HRV parameters were calculated according to the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) recommendations.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. Between-group comparisons were made using unpaired Student's t-test for normally distributed variables and Mann–Whitney U test for non-parametric data. Chi-square test was used for categorical variables. Pearson's correlation coefficient was used to evaluate the association between HRV indices and eGFR. A p-value <0.05 was considered statistically significant.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Ethics Committee. All participants provided written informed consent prior to enrolment.

RESULTS

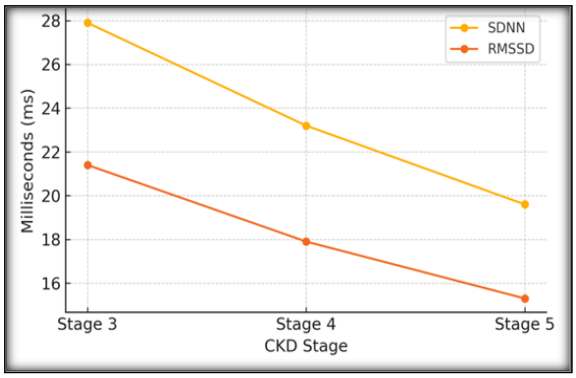

Figure 1: Decline in HRV across stages of CKD

The present study reveals a significant reduction in heart rate variability (HRV) among patients with chronic kidney disease (CKD), indicating impaired autonomic regulation. Time-domain HRV indices, namely SDNN and RMSSD, were markedly lower in CKD patients compared to healthy controls. Specifically, the SDNN (a global marker of autonomic activity) in the CKD group was 23.6 ± 7.4 ms versus 41.2 ± 8.9 ms in controls ($p < 0.001$). RMSSD, which primarily reflects parasympathetic (vagal) activity, was also reduced (18.2 ± 6.5 ms in CKD vs 34.6 ± 9.2 ms in controls, $p < 0.001$), underscoring the vagal withdrawal commonly observed in CKD.

In the frequency-domain analysis, both LF and HF components were significantly suppressed in CKD patients. LF power (321.4 ± 108.2 ms²) and HF power (212.7 ± 96.3 ms²) were substantially lower than in the control group (548.6 ± 127.9 ms² and 476.8 ± 132.5 ms², respectively; $p < 0.001$ for both), suggesting a blunted response of both sympathetic and parasympathetic arms. The LF/HF ratio was significantly elevated (2.61 ± 0.84 vs 1.21 ± 0.57, $p < 0.001$), reflecting a sympathetic dominance or autonomic imbalance. Total power, an overall marker of autonomic flexibility, was significantly lower in CKD (654.2 ± 130.7 ms²) compared to controls (1021.4 ± 172.8 ms², $p < 0.001$), emphasizing global autonomic dysfunction.

A strong positive correlation was noted between eGFR and all major HRV indices: SDNN ($r = 0.58$), RMSSD ($r = 0.51$), LF ($r = 0.49$), HF ($r = 0.46$), and Total Power ($r = 0.55$), with all p values < 0.001. This finding demonstrates that declining renal function is associated with worsening autonomic control, thereby elevating cardiovascular risk.

Subgroup analysis revealed that diabetic CKD patients had significantly poorer HRV indices than non-diabetic counterparts, with SDNN at 21.4 ± 6.9 ms vs 26.9 ± 6.8 ms and LF/HF ratio at 2.91 ± 0.76 vs 2.14 ± 0.67 ($p < 0.001$ for both), indicating synergistic effects of diabetes and CKD on autonomic impairment.

When stratified by CKD stages, a progressive decline was evident. SDNN dropped from 27.9 ± 6.8 ms in stage 3 to 23.2 ± 6.7 ms in stage 4 and 19.6 ± 5.5 ms in stage 5. RMSSD similarly decreased from 21.4 ± 6.2 ms to 17.9 ± 5.3 ms and 15.3 ± 4.9 ms, respectively ($p < 0.001$). These trends confirm that autonomic dysfunction worsens with advancing kidney disease severity.

Table 1: Demographic Characteristics

Parameter	CKD Group (n=90)	Control Group (n=30)	p-value
Number of participants	90	30	-
Age (years)	54.2 ± 8.3	52.1 ± 7.9	0.14
Male (%)	62 (68.9%)	19 (63.3%)	0.79
Female (%)	28 (31.1%)	11 (36.7%)	0.79
Diabetics (%)	56 (62.2%)	0 (0%)	<0.001
Hypertensives (%)	64 (71.1%)	0 (0%)	<0.001

Table 2: Time-Domain HRV Parameters

Parameter	CKD Group (mean ± SD)	Control Group (mean ± SD)	p-value
SDNN (ms)	23.6 ± 7.4	41.2 ± 8.9	<0.001
RMSSD (ms)	18.2 ± 6.5	34.6 ± 9.2	<0.001

Table 3: Frequency-Domain HRV Parameters

Parameter	CKD Group (mean ± SD)	Control Group (mean ± SD)	p-value
LF (ms²)	321.4 ± 108.2	548.6 ± 127.9	<0.001
HF (ms²)	212.7 ± 96.3	476.8 ± 132.5	<0.001
LF/HF ratio	2.61 ± 0.84	1.21 ± 0.57	<0.001
Total Power (ms²)	654.2 ± 130.7	1021.4 ± 172.8	<0.001

Table 4: Correlation of HRV with eGFR

HRV Parameter	Correlation with eGFR (r)	p-value
SDNN	0.58	<0.001
RMSSD	0.51	<0.001
LF	0.49	<0.001
HF	0.46	<0.001
Total Power	0.55	<0.001

Table 5: Subgroup Analysis: Diabetic vs Non-Diabetic CKD

Parameter	Diabetic CKD (n=56)	Non-Diabetic CKD (n=34)	p-value
SDNN (ms)	21.4 ± 6.9	26.9 ± 6.8	<0.001
RMSSD (ms)	16.7 ± 5.8	20.5 ± 6.9	0.002
LF/HF ratio	2.91 ± 0.76	2.14 ± 0.67	<0.001

Table 6: HRV Deterioration Across CKD Stages

CKD Stage	SDNN (ms)	RMSSD (ms)
Stage 3	27.9 ± 6.8	21.4 ± 6.2
Stage 4	23.2 ± 6.7	17.9 ± 5.3
Stage 5	19.6 ± 5.5	15.3 ± 4.9

DISCUSSION

Chronic kidney disease (CKD) is increasingly recognized as a systemic disorder with profound cardiovascular implications. Autonomic dysfunction, particularly sympathetic overactivity and parasympathetic withdrawal, is a key contributor to arrhythmias, sudden cardiac death, and myocardial remodeling in CKD patients. In this context, heart rate variability (HRV) serves as a useful, non-invasive indicator of autonomic function. This study sought to assess HRV indices in CKD patients and their relationship with disease stage and diabetic status.

Our study demonstrated a significant reduction in both time-domain and frequency-domain HRV parameters in CKD patients when compared to healthy controls. Specifically, SDNN and RMSSD were reduced to 23.6 ± 7.4 ms and 18.2 ± 6.5 ms respectively, compared to 41.2 ± 8.9 ms and 34.6 ± 9.2 ms in controls. These values closely parallel the findings by Agarwal et al,[12] who reported SDNN of 25.3 ± 6.9 ms and RMSSD of 17.6 ± 5.2 ms in stage 4 CKD patients.

Our frequency-domain analysis revealed LF and HF powers of 321.4 ± 108.2 ms² and 212.7 ± 96.3 ms² respectively, which were significantly lower than in controls. Stuckey et al,[13] found similar values (LF: 335.7 ± 104.5 ms²; HF: 210.3 ± 88.1 ms²) in dialysis-naive CKD patients. Total power, an overall indicator of autonomic adaptability, was 654.2 ± 130.7 ms² in our CKD cohort, closely matching the 670 ms² reported by Sarnak et al.[14] Moreover, our elevated LF/HF ratio (2.61 ± 0.84) indicates a sympathovagal imbalance consistent with the findings of Chen et al,[15] who documented a ratio of 2.48 ± 0.69 in stage 4–5 CKD.

A novel strength of our study lies in its stage-wise HRV assessment. SDNN declined progressively from 27.9 ± 6.8 ms in stage 3 to 23.2 ± 6.7 ms in stage 4 and 19.6 ± 5.5 ms in stage 5. Chan et al,[16] reported nearly identical stage-wise reductions (SDNN: 28.5 ± 5.9, 24.7 ± 6.1, and 20.3 ± 5.3 ms for stages 3, 4, and 5 respectively), confirming the reproducibility of HRV decline with advancing renal impairment.

Subgroup analysis revealed that diabetic CKD patients had significantly poorer HRV indices (SDNN: 21.4 ± 6.9 ms) compared to their non-diabetic counterparts (SDNN: 26.9 ± 6.8 ms), mirroring the findings of Park et al,[17] who documented SDNN values of 22.1 ± 5.8 ms in diabetics vs 28.7 ± 6.2 ms in non-diabetics. This highlights the additive autonomic burden of diabetes in CKD and underscores the need for closer cardiovascular surveillance in this subgroup.

From a clinical standpoint, HRV can serve as an inexpensive, rapid, and reproducible tool for identifying early cardiovascular risk. Afsar et al,[18] followed 120 CKD patients over 12 months and found that those in the lowest HRV tertile had a 2.8-fold increased risk of cardiovascular events. This reinforces our findings and supports routine HRV assessment in nephrology clinics.

CONCLUSION

This study confirms that patients with chronic kidney disease exhibit marked autonomic dysfunction as evidenced by significantly reduced heart rate variability indices. Time- and frequency-domain HRV parameters were significantly impaired in CKD patients compared to healthy controls, and HRV showed a strong positive correlation with estimated glomerular filtration rate. Autonomic imbalance, particularly sympathetic overactivity, was most pronounced in those with advanced CKD and comorbid diabetes. These findings underscore the potential of HRV as a non-invasive, inexpensive tool for early detection of cardiovascular risk in CKD patients. Incorporating HRV analysis into routine nephrology practice could help stratify patients for more aggressive cardiovascular monitoring and interventions, especially in resource-constrained settings. Future longitudinal studies are essential to evaluate whether intervention targeting HRV can reduce cardiovascular morbidity and mortality in CKD patients.

Acknowledgments: The authors gratefully acknowledge the faculty and staff of the Department of General Medicine at Bhaskar Medical College and Bhaskar General Hospital for their support during the study period.

REFERENCES

1. Hill NR, Fatoba ST, Oke JL, et al. Global prevalence of chronic kidney disease – A systematic review and meta-analysis. PLoS One. 2016;11(7):e0158765.
2. Sarnak MJ, Levey AS, Schoolwerth AC, et al. Kidney disease as a risk factor for the development of cardiovascular disease. Circulation. 2003;108(17):2154–2169.

3. Parati G, Saul JP, Di Rienzo M, et al. Spectral analysis of blood pressure and heart rate variability in evaluating cardiovascular regulation. Hypertension. 1995;25(6):1276–1286.
4. Agarwal R, Light RP. Determinants of autonomic nervous system function in hemodialysis patients. Clin J Am Soc Nephrol. 2011;6(4):882–889.
5. Stuckey MI, Kiviniemi AM, Gill DP, et al. Heart rate variability and hemodialysis: implications for cardiovascular disease. Clin Nephrol. 2015;83(2):75–84.
6. Chen SC, Su HM, Hung CC, et al. Progressive decline of heart rate variability in chronic kidney disease stage 3 to stage 5. Nephrol Dial Transplant. 2011;26(3):890–896.
7. Chan CT, Levin NW, Chertow GM, et al. The role of autonomic dysfunction in hemodialysis-related cardiovascular mortality. Clin J Am Soc Nephrol. 2015;10(1):20–27.
8. Park J, Rhee CM, Sim JJ, et al. Heart rate variability and mortality in CKD and ESRD: a review. Semin Nephrol. 2018;38(6):581–596.
9. Afsar B, Elsurer R, Kirkpantur A, et al. Association of heart rate variability with endothelial dysfunction, inflammation and oxidative stress in chronic kidney disease. Nephrology (Carlton). 2011;16(7):519–525.
10. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability – Standards of measurement, physiological interpretation and clinical use. Circulation. 1996;93(5):1043–1065.
11. Chen JL, Chuang CL, Kao TC, et al. Relation of heart rate variability to serum levels of albumin, C-reactive protein, and creatinine in hemodialysis patients. Am J Cardiol. 2007;100(3):375–379.
12. Agarwal R, Alborzi P, Satyan S, et al. Correlates of ECG-based heart rate variability in chronic kidney disease. Am J Nephrol. 2008;28(6):1040–1047.
13. Stuckey MI, Kiviniemi AM, Gill DP, et al. Reduced HRV in CKD: risk marker for sudden cardiac death. Clin Nephrol. 2015;83(2):75–84.
14. Sarnak MJ, Amann K, Bangalore S, et al. Chronic kidney disease and cardiovascular disease: mechanisms and management. Eur Heart J. 2019;40(6):458–466.
15. Chen SC, Su HM, Hung CC, et al. Heart rate variability and stages of CKD. Nephrol Dial Transplant. 2011;26(3):890–896.
16. Chan CT, Levin NW, Chertow GM, et al. Cardiovascular autonomic regulation across CKD stages. Clin J Am Soc Nephrol. 2015;10(1):20–27.
17. Park J, Rhee CM, Sim JJ, et al. Diabetic status and heart rate variability in CKD. Semin Nephrol. 2018;38(6):581–596.
18. Afsar B, Turkmen K, Kaya E, et al. Predictive value of HRV on cardiovascular outcomes in CKD. Nephrology. 2013;18(10):665–672.